

If Cumulative Risk is the Answer, What is the Question?

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Principal Science Issue

- Individuals and communities can have differential risk of adverse health effects, even with comparable exposure, depending upon additional stressors and vulnerability factors
- Risk guidance is needed to link chemical and non-chemical stressors in a consistent manner when assessing both human and ecological health

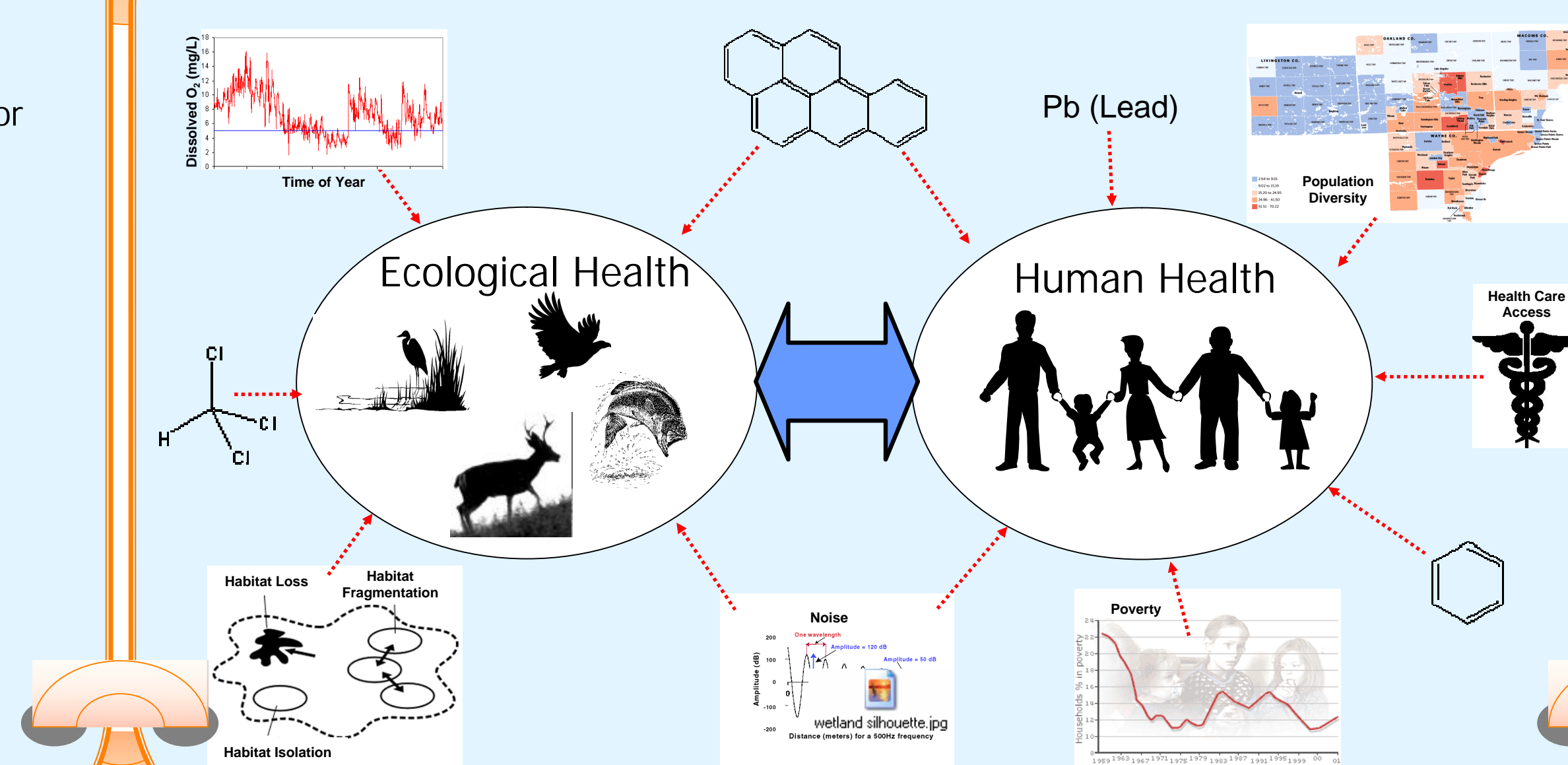
Objective

- Address important theoretical issues that were identified in the *Framework for Cumulative Risk Assessment* as needing exploration

Approaches for Assessing Combined Effects from Multiple Stressors

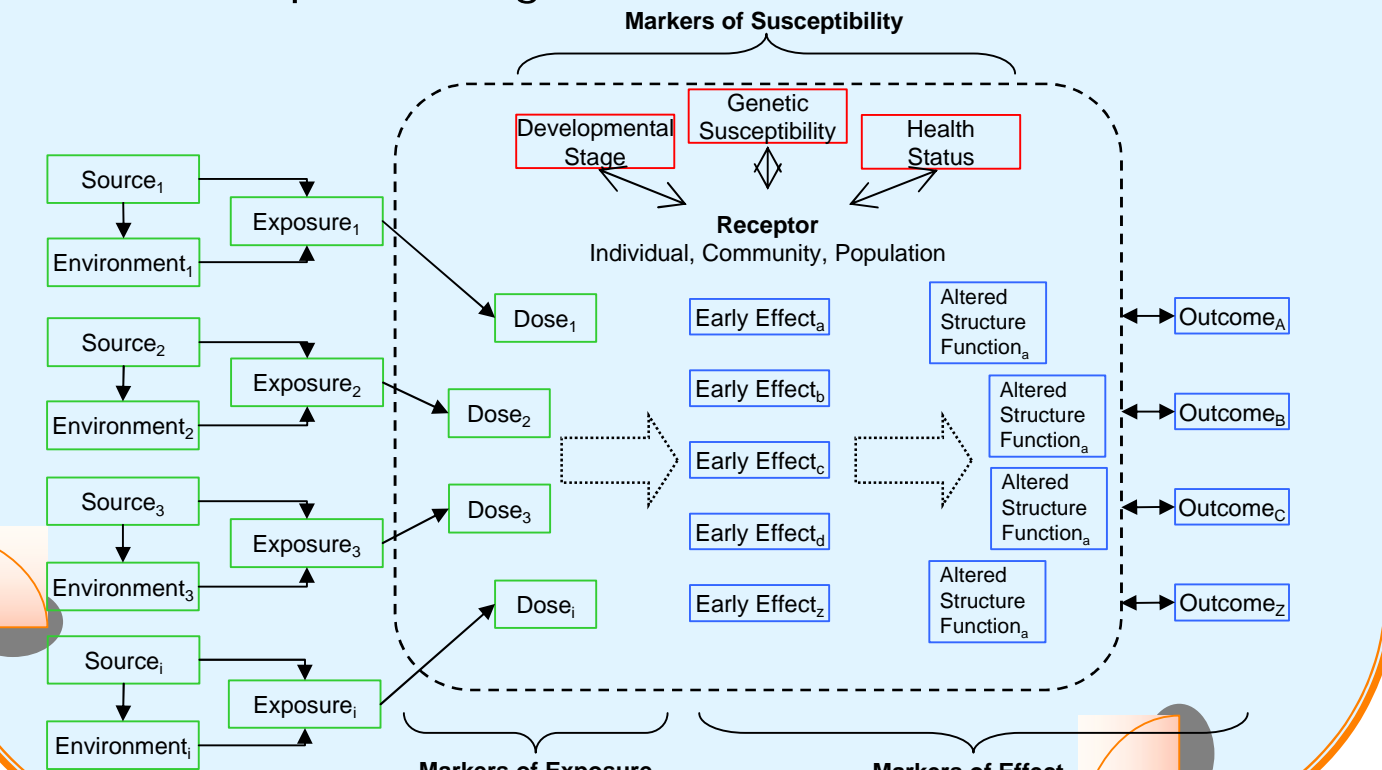
- Provides a conceptual overview on how to assess combined effects from multiple stressors, and the types of stressors and effects that may be combined, such as physical, biological, and chemical stressors. The types and nature of the interactions among these various stressors that may be needed to assess effects were compiled and defined, including both adverse and beneficial outcomes
- The approaches for combining effects included
 - interactive conceptual models, typically used for capturing important elements and posing hypotheses
 - screening methods, typically for reducing the number of stressors by focusing on most important variables contributing to effects
 - analytic methods, typically more complex approaches that combined multiple methods such as advanced statistical techniques and process models.
- Discusses the significance of the exposure groups for both human health and ecological risk assessments and/or ecological systems for ecological risk assessments

CUMULATIVE RISK ASSESSMENT



Using Biomarkers to Inform Cumulative Risk Assessment

- Biomarkers can reflect cumulated influences or exposures and can add significantly to environmental health studies.
- Ideally a biomarker should be persistent, be easily collected, be reliable, and be linked to a disease, however it is recognized that an array of biomarkers is more useful in disaggregating sources and pathways of exposure, and may have applications in tracking disease burden.
- A cumulative framework was developed and applied to asthma (e.g., associated with VOCs, ETS, PM), neurobehavioral endpoints (e.g. associated with mercury, lead, and organic solvents exposure), multifactorial effects (e.g., developmental and reproductive disorders), and endocrine disrupting effects upon ecological communities.

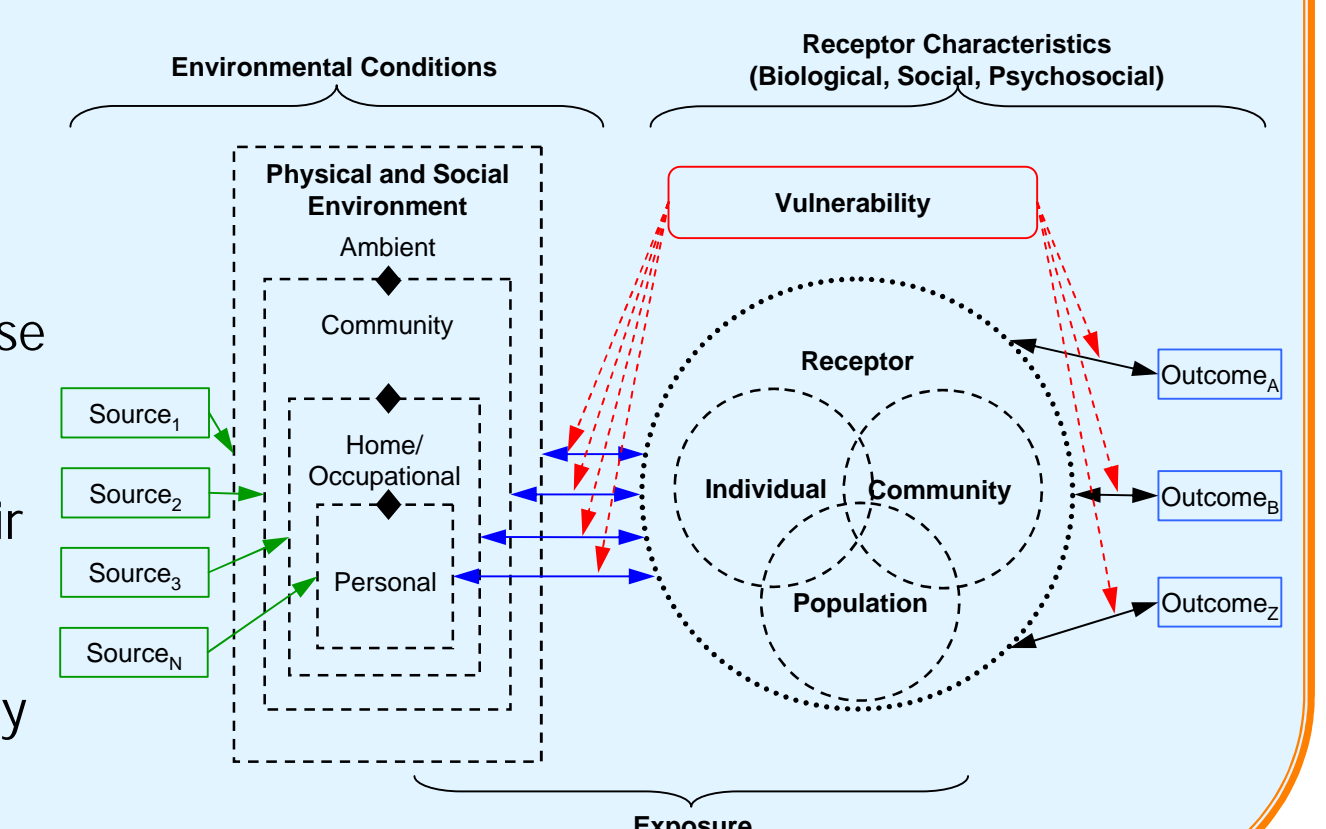


The Challenge of Assessing Cumulative Exposure and Related Combined Effects

- Discusses how differential exposure to mixtures of environmental agents, including biological, chemical, physical, and psychosocial stressors, can contribute to increased vulnerability of human populations and ecological systems
- Describes which mixtures are most important from a public health perspective
- Discusses the nature and magnitude of relevant cumulative exposures
- Describes the nature and magnitude of the mixture's interactive effects on exposed populations
- Reinforces the need for improved assessment of cumulative exposure and better biological mechanisms that determine toxicological interactions among mixture constituents

Vulnerability as a Function of Individual and Group Resources in a Cumulative Risk Assessment

- Discusses vulnerability as it relates to how individuals or groups of individuals or organisms react to and recover from stressors
- Focuses on non-chemical stressors, such as psychosocial stress, community structure and function, and population assessment and response
- Describes factors that affect how a person, animal, an ecological population or community might be more or less vulnerable because of their capacities and resources, coping mechanisms, supports, or size and complexity of the group
- Describes metrics to qualitatively or quantitatively assess individual, community or ecosystem vulnerability



Discussion

- Several issue papers (blue boxes) were developed on key concepts that may assist in performance cumulative risk assessments:
- Current methodologies for combining multiple stressors are inadequate for quantifying cumulative effects.
 - Arrays of biomarkers, combined with additional knowledge of PK and PD activity of chemicals in mixtures and a low levels, are needed to quantify cumulative effects
 - Combinations of stressors can cause cascading effects that can be detected for human or ecosystem communities, affecting overall estimate of risk
 - Metrics are proposed for qualitative and quantitative assessment of vulnerability of ecosystems and communities

Conclusion

Collaboration – both within and outside EPA -- has resulted in progress in dealing with the significant scientific challenges for developing ways to do Cumulative Risk Assessment. These include sorting out the role of various stressors/factors and their interactions, and developing tools. The issue papers will help us meet that challenge.

Future Research Areas

- Use of biomarkers, including gene arrays, for detection of effects from mixtures of environmental stressors
- Identification and validation of metrics of vulnerability to environmental stressors and development of an universal metric to combine chemical and non-chemical stressors
- Develop cumulative risk assessment guidance

Cumulative Risk Assessment Technical Panel Members

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